

Status Summary

Claims 1-11 are pending in the present application and have been examined by the U.S. Patent and Trademark Office (hereinafter "the Patent Office"). Claims 1-5, 9 and 10 have previously been withdrawn. Claims 6-8 and 11 presently stand rejected.

Claims 6-8 and 11 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are incomplete for omitting essential steps.

Claims 6-8 and 11 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims fail to comply with the written description requirement.

Claims 6-8 and 11 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims lack enablement.

Claims 6, 8 and 11 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by European Patent No. EP 1,184,665 to Ogawa et al. (hereinafter "Ogawa et al.").

By this Amendment, claims 6, 7, and 11 have been amended. No new matter has been added. Therefore, upon entry of the Amendment, claims 6-8 and 11 will be pending in the subject application.

Response to the Rejection of Claims Under 35 U.S.C. § 112, second paragraph

Claims 6-8 and 11 have been rejected under 35 U.S.C. § 112, second

paragraph, upon the contention that the claims are incomplete for omitting essential steps. The Patent Office contends that the omitted steps are: a step or several steps defining how the protein kinase activity is measured and a result of the determining step, i.e. is an increase or decrease in DNA-dependent protein kinase activity indicative of cancer.

The positions of the Patent Office as summarized above with respect to the rejected claims are respectfully traversed as described below.

Initially, applicants respectfully disagree with the Patent Office regarding the contention that the claims must recite one or more steps defining how the protein kinase activity is measured. In particular, applicants respectfully note page 12, lines 2-6 of the instant specification which recites, "The method for measuring DNA-dependent protein kinase activity is described hereinbefore, but the present invention is not limited to this. Any method for measuring DNA-dependent protein kinase activity is within the scope of the present invention.". As such, applicants respectfully submit that the means by which DNA-dependent protein kinase is measured is not limited to the methods described in the specification and appropriate alternative methods are believed to be within the skill of one of ordinary skill in the art. Therefore, this portion of the instant rejection is believed to be improper.

However, assuming *arguendo* that this portion of the instant rejection is proper, applicants respectfully submit that claims 6, 7, and 11 have been amended to further clarify the claimed subject matter. Specifically, claims 6, 7, and 11 have been amended to recite, *inter alia*, "a method for assessing a subject's susceptibility to

cancer to determine if the subject is prone to cancer, wherein the measuring comprises detecting the radioactivity of a peptide substrate phosphorylated by the DNA-dependent protein kinase activity of the cells in the presence of a radiolabeled phosphate compound". Support for the amendments can be found throughout the specification, including particularly in the specification as originally filed at page 9, line 14 through page 11, line 3. Thus, no new matter has been added by the amendments to claims 6, 7, and 11.

Accordingly, applicants respectfully submit that the Patent Office's contention that the instant claims must include a step or several steps defining how the protein kinase activity is measured is believed to have been addressed. As such, applicants respectfully request withdrawal of this portion of the instant rejection.

Regarding the second part of the instant rejection, applicants respectfully disagree that the claims must recite that the DNA-dependent protein kinase activity is either increased or decreased. Applicants respectfully submit that when viewed in light of the specification, the meaning of the claims regarding the relationship between DNA-dependent protein kinase activity and cancer susceptibility is believed to be clear. See, for example, M.P.E.P. § 2111, which recites, *inter alia*, "During patent examination, the pending claims must be given their broadest reasonable interpretation consistent with the specification.". Further, applicants respectfully submit that one of ordinary skill in the art, upon review of the instant disclosure, will be well apprised of the intended meaning of the claims. In particular, applicants respectfully submit that the specification clearly states, at page 11, line 13; page 12,

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line 8; page 15, line 17; page 16, lines 10 and 17; page 23, lines 4, 8, and 10; and page 24, line 13, that cancer susceptibility is increased when DNA-dependent protein kinase activity is decreased or lower. Accordingly, applicants respectfully submit that this portion of the instant rejection is believed to have been addressed.

Of note, applicants respectfully submit that claim 7, as amended in the previous response to the second Official Action (Amendment B), recites, *inter alia*, “wherein a lower DNA-dependent protein kinase activity for the test subject indicates an increased likelihood of developing cancer.”

Accordingly, applicants respectfully submit that claims 6-8 and 11 are believed to be in compliance with 35 U.S.C. § 112, second paragraph. Thus, applicants respectfully request that the rejection of claims 6-8 and 11 under 35 U.S.C. § 112, second paragraph, be withdrawn, and request that claims 6-8 and 11 be allowed at this time.

Response to the Rejection of Claims Under 35 U.S.C. § 112, first paragraph,
for Failure to Comply with the Written Description Requirement

Claims 6-8 and 11 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims fail to comply with the written description requirement. The Patent Office contends that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Patent Office asserts that the

phrase "further screened for cancer" is not supported in the specification as filed and is therefore considered new matter.

The positions of the Patent Office as summarized above with respect to the rejected claims are respectfully traversed as described below.

Initially, applicants respectfully submit that support for the phrase "further screened for cancer" can be found, for example, at page 16, lines 6-15, as indicated at page 7 of the previously filed Amendment B. In particular, at page 16, lines 12-15, the specification recites, "Therefore, the method can be used for selecting subjects to be examined for cancer screening more selectively from healthy subjects.". According to M.P.E.P. 2163.02, "The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement." Rather, per M.P.E.P. 2163.02, "An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).". As such, upon review of the instant specification, applicants respectfully submit that one of ordinary skill in the art will be well apprised that the presently disclosed and claimed subject matter is directed to methods of assessing a subject's susceptibility to cancer to determine if the subject should be further screened for cancer. Stated another way, it is believed that one of ordinary skill in the art will understand that if an assessment of a subject's susceptibility to cancer suggests he or she is likely to develop cancer, then further

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cancer screening may be employed by a medical practitioner to clarify the subject's cancer risk. As such, applicants respectfully submit that the phrase "further screened for cancer" is not believed to constitute new matter.

However, without acquiescing to the contentions of the Patent Office and in an effort to further prosecution, applicants respectfully submit that claims 6, 7 and 11 have been amended herein by replacing the phrase "further screened for cancer" with the phrase "is prone to cancer". Support for the instant amendments can be found throughout the specification as originally filed and particularly at page 16, lines 6-15. No new matter has been added.

Accordingly, applicants respectfully submit that claims 6-8 and 11 are believed to be in compliance with the written description requirement of 35 U.S.C § 112, first paragraph. Thus, applicants respectfully request that the rejection of claims 6-8 and 11 under the written description provision of 35 U.S.C. § 112, first paragraph, be withdrawn, and request that claims 6-8 and 11 be allowed at this time.

Response to the Rejection of Claims Under 35 U.S.C. § 112, first paragraph,
for Lack of Enablement

Claims 6-8 and 11 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims lack enablement. The Patent Office contends that there is no guidance to assist one of skill in the art in predicting a patient's susceptibility to cancer by measuring protein kinase activity and that the measurement of protein kinase activity is not indicative of cancer. The Patent Office also contends that the specification does not correlate protein kinase activity with genetic mutations and the development of cancer. Finally, the Patent Office alleges that Someya et al. (of record) argues against evidence that the amount of protein kinase activity relates to the amount of genetic mutations and thus the development of cancer.

The positions of the Patent Office as summarized above with respect to the rejected claims are respectfully traversed as described below.

The Patent Office first asserts that there is no guidance to assist one of skill in the art in predicting the susceptibility of a patient to cancer by measuring protein kinase activity and that the measurement of protein kinase activity is not indicative of cancer. This assertion appears to be based, at least in part, upon the notion that data presented in the instant application is from patients who already have cancer, not from patients who have yet to be diagnosed with cancer. Further, the Patent Office appears to use findings reported by Someya et al. to support the contention that protein kinase activity is not indicative of cancer.

Initially, applicants respectfully submit that the Patent Office appears to have mischaracterized the teachings of Someya et al. While Someya et al. may report that there were no significant differences in DNA-dependant protein kinase activity between normal controls and patients suffering from head and neck cancer, esophageal cancer and malignant lymphoma in that particular study, this does not support the Patent Office's broad conclusion that protein kinase is not indicative of cancer. In marked contrast, Someya et al. report that DNA-dependent protein kinase activity is associated with the risk of breast and uterine cancer. See, for example, the abstract, page 121 and page 122, of Someya et al. Further, the Patent Office, at page 4 of the Official Action, states that data from Someya et al. argues against evidence that the amount of protein kinase activity relates to the amount of genetic mutations and thus the development of cancer. However, applicants respectfully submit that this is an inaccurate summary of Someya et al. Rather, Someya et al. concludes just the opposite. See, for example, page 122, which recites, "In conclusion, our data suggests that DNA-PK activity is associated with chromosomal instability and risk of cancer. Therefore, DNA-PK activity in PBL can be used to select individuals from whom an examination should be performed because of their increased susceptibility to cancer." (emphasis added). As such, the Patent Office appears to be making broad and erroneous conclusions based upon a selective reading of Someya et al.

Additionally, applicants respectfully submit that the design of the study reported by Someya et al. may have precluded the realization of a statistically

significant difference in the DNA-PK activity. In particular, because the number of patients with head and neck cancer (20 patients), esophageal cancer (6 patients) or malignant lymphoma (5 patients) was substantially smaller than that of the control (41 patients) and breast cancer (38 patients) groups, the disparity may have precluded the recognition of a statistically significant difference in the DNA-PK activity in peripheral blood lymphoid cells of these patients.

Further, applicants respectfully submit that claims 6, 7, and 11 have been amended to further clarify the claimed subject matter. Specifically, claims 6, 7, and 11 have been amended by deleting the recitation of head and neck cancer. No new matter has been added. As such, applicants respectfully submit that the claims are directed to breast cancer and uterine cancer, both of which are supported by the instant disclosure as well as the Someya et al. reference.

Regarding the Patent Office's contention that the specification does not provide any direction or guidance to assist one skilled in the art in the determination of susceptibility to cancer before the patient has the cancer because the data of the instant application is from patients already diagnosed with cancer, applicants respectfully disagree. Initially, applicants respectfully submit that the Patent Office has identified no sound scientific basis for the assertion that the specification does not reasonably provide enablement for determining cancer susceptibility in patients who have not yet been diagnosed with cancer. According to *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971):

As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi at page 223 (emphasis added).

Furthermore, according to the Training Materials for Examining Patent Applications with Respect to 35 U.S.C. Section 112, First Paragraph-Enablement Chemical/Biotechnical Applications “the case law makes clear that properly reasoned and supported statements explaining any failure to comply with Section 112 are a requirement to support a rejection”. *Citing In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Applicants respectfully submit that only general assertions have been made and that no such “properly reasoned and supported statements” have been presented. As a result, applicants respectfully submit that the Patent Office has not satisfied its burden concerning the establishment of a *prima facie* case of lack of enablement of claims 6-8 and 11.

However, assuming *arguendo* that the Patent Office has established a *prima facie* case of lack of enablement, applicants respectfully submit that the instant claims directed to assessing a subject’s susceptibility to cancer are not limited to patients already diagnosed with cancer. Applicants reiterate that one of ordinary skill in the art is well apprised of the notion that chromosome abnormalities are the result of damages to DNA molecules that result in genetic mutations and that the accumulation of genetic mutations can lead to malignant transformations in cells,

resulting in cancer. See, for example, page 7, lines 8-17 of the specification. Further, DNA-dependent protein kinase plays a role in preventing genetic mutations and chromosome abnormalities. See, for example, page 3, lines 6-13 and Figure 1, which illustrates that chromosome abnormalities are inversely related to DNA-dependent protein kinase activity. Therefore, a decrease in DNA-dependent protein kinase activity that results in an increase in chromosome abnormalities can result in increased susceptibility to cancer. As such, a subject with decreased DNA-dependent protein kinase activity, determined in accordance with the presently disclosed subject matter, is susceptible to, or has an increased likelihood of, developing cancer due to an increased potential to develop genetic mutations. See page 15, line 10, through page 16, line 15.

Thus, since it is established that DNA-dependent protein kinase is inversely related to genetic mutations and that genetic mutations can lead to cancer, it is axiomatic that prior to the development of cancer resulting from genetic mutations there must have been present one or more genetic mutations. Stated another way, cancer resulting from one or more genetic mutations cannot develop unless there is first a genetic mutation. As such, one of skill in the art will appreciate that the relationship between cancer, genetic mutations and DNA-dependent protein kinase activity exists both pre and post-cancer development. Additionally, Someya et al., which clearly supports the relationship between DNA-dependent protein kinase activity and susceptibility to breast and uterine cancer, as presently claimed, is also

based upon data from subjects already diagnosed with cancer. See, for example, the last paragraph on page 122, of Someya et al.

To elaborate, while the DNA-PK activity disclosed herein was derived from cancer patients, the decreased DNA-PK activity is not believed to be a result of the cancer itself. Rather, researchers have revealed that the activity of DNA-PK is only influenced by the amount of mRNA encoding DNA-PK and the amount of DNA-PK protein. It is further known that a single nucleotide polymorphism of the DNA-PK gene may contribute to these mRNA and protein concentrations. Consequently, it is recognized that genetically determined factors influence DNA-PK activity. As such, it is believed that a reduction in DNA-PK in cells from cancer patients is caused before the development of the cancer, not caused by the cancer.

Finally, the Patent Office asserts that while genetic mutations are involved in a number of cancers, they are not the sole cause of cancer, nor the sole determinant of whether a person will develop cancer. See, page 5 of the Official Action. In response, applicants respectfully submit that nowhere do the claims recite that DNA-dependent protein kinase activity is the sole cause of cancer or the sole determinant of cancer. Rather, the claims are directed to methods of assessing a subject's susceptibility to cancer to determine if the subject should be further screened for cancer. As such, the intention of the presently claimed subject matter is not to predict that a subject will develop cancer, but rather, to provide a method of screening subjects to determine if, based upon DNA-dependent protein kinase activity, a patient is more or less likely to develop cancer. As such, the Patent

Office's reasoning for the lack of enablement rejection does not fall within the context of the claimed subject matter. Further, the clearly established correlation between DNA-dependent protein kinase activity and cancer susceptibility based upon genetic mutations fully enables the instant claims.

Accordingly, applicants respectfully submit that claims 6-8 and 11 are enabled by the specification in accordance with 35 U.S.C § 112, first paragraph, regarding the ability to assess a subject's susceptibility to cancer to determine if the subject is prone to cancer. Thus, applicants respectfully request that the rejection of claims 6-8 and 11 under 35 U.S.C. § 112, first paragraph, be withdrawn, and request that claims 6-8 and 11 be allowed at this time.

Response to the Rejection of Claims Under 35 U.S.C. § 102(b)

Claims 6, 8 and 11 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by European Patent Application Publication No. EP 1,184,665 to Ogawa et al. (hereinafter "Ogawa et al."). The Patent Office contends that Ogawa et al. teach a method for measuring protein kinase activity in a test sample consisting of the steps of contacting the sample with a substrate peptide phosphorylated by the protein kinase under conditions necessary for the phosphorylation reaction and detecting a change in the phosphorylation level of the substrate peptide based on the change in reactivity of the substrate peptide with an antibody that identifies the phosphorylation site of the substrate peptide, wherein the sample is obtained from tissue samples, blood, urine, body fluids, sweat, saliva, and

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body secretions such as milk. Further, the Patent Office contends that since the only active step of the claimed method is measuring protein kinase activity and Ogawa et al. teach measuring protein kinase activity, all of the limitations of the claims have been met.

The positions of the Patent Office as summarized above with respect to the rejected claims are respectfully traversed as described below.

In response, applicants respectfully submit that claims 6 and 11 have been amended as discussed hereinabove. In particular, claims 6 and 11 have been amended to recite, *inter alia*, "...wherein the measuring comprises detecting the radioactivity of a peptide substrate phosphorylated by the DNA-dependent protein kinase activity of the cells in the presence of a radiolabeled phosphate compound...". Applicants respectfully submit that Ogawa et al. does not teach or suggest a method for assessing a subject's susceptibility to cancer by measuring DNA-dependent protein kinase activity, wherein the measuring comprises detecting the radioactivity of a peptide substrate phosphorylated by the DNA-dependent protein kinase activity of the cells in the presence of a radiolabeled phosphate compound as recited in the instant claims. As such, applicants respectfully submit that Ogawa et al. does not teach each and every element of the instant claims and therefore does not support a rejection of claims under 35 U.S.C. § 102(b).

Accordingly, applicants respectfully submit that the claims 6 and 11 are believed to be novel over Ogawa et al. Further, as claim 8 depends from claim 6, and therefore shares the novel features of claim 6, it too is believed to novel over

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Ogawa et al. Thus, applicants respectfully request that the rejection of claims 6, 8 and 11 under 35 U.S.C. § 102(b) be withdrawn, and request that claims 6, 8 and 11 be allowed at this time.

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CONCLUSION

In light of and upon entry of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Office has had an opportunity to review the above Remarks, the Patent Office is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

FEE DUE

A check in the amount of \$60.00 is enclosed for the fee due. The Commissioner is authorized to charge any deficiencies of payment associated with the filing of this correspondence to Deposit Account No. 50-0426 to avoid the unintentional abandonment of the instant application.

Respectfully submitted,

JENKINS, WILSON, TAYLOR & HUNT, P.A.

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